



Building a Collaborative Biomedical Network

Question and Answer Session from the caBIG® 2010 Annual Meeting Tuesday, September 14, 2010

Susan Love, M.D.

It was great to be here last year and talk to you, those of you who were here, about our project the Love Avon Army of Women. And I'm going to give you an update of where we are and where we're going and some of the new things that we're doing with that today. And more and more we're seeing this as a model of really democratizing research, taking it out of the ivory tower and really involving the public, both in the formulation of the research as well as accomplishing it. So the Dr. Susan Love Research Foundation is working to eradicate breast cancer, and we try to do this through innovative research, education, and advocacy. So we try to get rid of the barriers, explore new approaches, and really try to create new solutions. And our goal is to really go beyond the cure. I mean, a lot of the focus these days—and the pink October with its pink is on the horizon—is the cure, but we really would like to find the cause and just stop it once and for all.

The problem, as I see it, or one of the major problems certainly is the way we've been thinking about and doing research, clinical and otherwise, where you have the public, the public gets sick and becomes a patient and goes to the medical enterprise, and then the non-profit and the research enterprise are completely separated from this. This doesn't really get a lot done and it doesn't get it done in a very coordinated way. So you do research about things that really people don't think in the medical world are problems and you have medical problems that aren't being researched and the patients are left out in the cold.

The goal of the Love/Avon Army of Women is to try to accelerate the research by moving women into the process, getting beyond some of the animal models. So instead of just the investigator-initiated research where you've got scientists thinking up what they think would be interesting projects, we really include an alternative model where the public and the non-profits come up with some of the problems and issues that they would like to see dealt with and then facilitate them coming to the answer. So the problem is really how do you do this, how do you accelerate, initiate, facilitate research on clinical problems, get accessible biospecimens and data and people to be in the studies. It's all well and good to say we want people to do it, but if you don't make it—have a mechanism to do it, it's not going to happen.

Right now there are three models out there. There's the registry of people with disease, and this is the most common. And you see it with a lot of different diseases where you have the Myeloma Foundation or Michael J. Fox or Lance Armstrong where you collect information in a database from people with a disease, researchers come up with questions, solicit participants or data that match their criteria.



BreastCancerClinicalTrials.org is one method that does this. A woman could put all her information online and then if you're doing a clinical trial, you go in and match. Another is just a listing of studies, so now the participant just goes and looks at the list like a menu and picks out what they want. That's like Cancer.gov. And then finally we have our model which is an open database of people who are interested in participating in research which is the Army of Women.

So if you go back to my problem, now you've got the public becoming—you've got the classical non-profit here with my—this is Lance Armstrong or these where you—where they're collecting a registry from the patients and from the medical enterprise and they're sharing it with research and pharma. And then what we're proposing in the Army of Women is really, as I learned in business school, disintermediating the medical enterprise which I think gets in the way of research more often than not and having the public directly interact with a non-profit, the patient interact with a non-profit and the research, and not worry about the medical enterprise, let them do their own thing. And as a surgeon and a physician, I can disintermediate the medical enterprise since I'm part of that group.

So the difference between the two are if you have a registry, you have specific recruitment, whereas with an open database, it's open. You really end up collecting data on the things you already know, currently-recognized research factors, whereas with a open recruitment, you can take anybody who wants to be—healthy people, not just the people with the disease, and you can ask anything. You have a database and a registry for matching, you've got to keep it current, you've got to limit it to what's known, whereas in an open database, you can self select and not really collect any data, leave it with the people and it adapts very easily to new hypotheses. When you have a biobank from your registry, you end up saving the tissue with the technology of today and then there's a new technology and it turns out you saved it all in alcohol and it needed to be in saline. And so your whole biobank is worthless for the new technology. This way, we just leave everything in the women, there's no storage, and it's adaptable to new technologies.

The limitations are the registry's more expensive, it's a lot of work, and it can preclude discovering new information. And breast cancer we keep looking at the same risk factors over and over again. But in an open database, you have no ownership so that's a limitation but it is less expensive and it can accommodate both rare and common diseases.

So we started with a grant from the Avon Foundation, the Love/Avon Army of Women, and the idea is to encourage women to get involved in the next step. They've marched, they've walked, they've worn pink, and now to really participant in research to try to find the cause of breast cancer. It's really trying to forge a partnership between the women and the researchers and to move research more into prevention and then to get researchers to study clinically-important questions. So members sign up online, they receive email announcements of available studies, and then they self select. If they fit and they're interested, they RSVP, they go through an online screening, and then they're passed on to the researchers. Researchers submit their studies to us online, we approve them, and then after we get IRB approval for online recruiting, we put it out.



We have over 337,000 women in the Army of Women right now. Eighty percent are healthy, have not had breast cancer. Twenty percent are survivors. Thirty-five studies have been launched in the two—not quite two years. Seventeen were closed. Six studies increased their end, their recruitment, because we were so successful they said, "Oh, well, we had only asked for 250 but maybe we'll take a thousand after all." Many studies have reached full recruitment within a week, accelerating significantly the timeline. We have an active and growing scientific advisory committee of 20 members, a successful foot soldier program with over 1,200 women who are more active in recruiting new people to the Army, and lots of PR mentions that'll be coming up even more with October. And it's a partnership. The researchers have to present the data back to the women and the people who are in the study, either in person or in a webinar.

The kinds of studies we've done range from quality of life and psychosocial to chemo prevention, biomarkers, education studies. And I'll go through a few examples just to show you how this works. The BEAM Study is a study out of—that was both in Northwestern and Johns Hopkins launched in July 22 of last year, and it's using DNA methylation and you have to have a core biopsy—this is in healthy women—to provide individual and look for breast risk profiles. They needed 300 women and we got 300. We had 10,000 responses and 300 RSVPs for this study. They told us prior to using the Army of Women, at Northwestern University they had 51 women in 16 months, 23 of which came after the Army blast within a month. And in the Hopkins, again, 34 in five months all from the Army. So these are volunteers who are going to come in and have a core biopsy that they don't need just to be part of research. And they found all of them that came were highly motivated and most of them were, in fact, really eligible.

The sister study was a national study that still needed 5,000 more women looking at environment and genes out of the NIEH, and we were able to complete—they had been open for years, since 2002. We were, within two weeks, were able to get 2,300 and we got 5,000 within several months and they were able to close that study.

The milk study is an example of kits. This study needed women who were breastfeeding and scheduled for a breast biopsy. They would send you a kit, you put some milk in it, and you ship it back to them. But the number of women who are breastfeeding and need a breast biopsy is actually quite low. They wanted 250. In 24 hours we had 31 which already accelerated them six months. And to date we've given them 324. They've now gotten a little more greedy and said, "Well, this was so easy, let's have a thousand. We had figured out our end just based on the bare minimum and now that we know we can do it, let's do more."

Another study at UCLA looked for obese women. They needed 20 subjects. They had to have a controlled diet and exercise study and looking at markers. And we got 125 within 12 hours and complaints from Chicago, from Michigan saying, "We're fat here too. Can't we be in this study?"

And then this study out of Stanford, you had to have imaging, genetic markers, neuropsychological testing, MRIs, all for cognitive defects with chemo brain. 180



women required and a 1,314 were recruited. People were willing to fly in on their own dime to Stanford to be part of this study.

This showing you is another type of study, University of Southern California, the grapefruit study. Sixty-five women needed. They had to eat grapefruits every day for six months and have blood draws once a week, and it was a complicated study. But 203 were easily recruited in southern California and they were able to close the study within two days, their recruitment.

And then this study just shows that we're good at minority groups or less common groups. This is out of Boston. They were looking at the health needs of lesbians. They needed 100 lesbian and bisexual women; we were able to get them 158 very quickly and move that study along. And a second study here looking at fertility concerns in women with breast cancer had no African Americans. So we put it out just to the recruit the African Americans for that study and got them 20 within a short period of time and made it a much more robust study.

The next step now for the Army—I mean, we're continuing with the Army and anyone who has studies, please—or wants to be in the Army, please participate. But the biggest complaint we get from the Army of Women is not enough things for me, you know, I haven't found a study for me yet. And so this led us to come up with the Health of Women study, or HOW. And the idea of the Health of Women study is both to collect information over time online but also educate women in the research process by engaging them in figuring this out. It's a partnership with City of Hope, Leslie Bernstein, and Katherine Henderson and caBIG[®] and the Dr. Susan Love Research Foundation, and it's an online cohort study with periodic modules and questions to engage the — that'll engage the public. The purpose is to accelerate the process of data collection and access the research process, accelerate the research process. So we're trying to, instead of doing it the way a traditional cohort is where you send out a 16-page questionnaire every couple of years, just have very short modules that will take you 15 minutes to do every couple of months and collect data on an ongoing way. It gives all the members of the Army a chance to participate in research and see how it's done.

So we'll have two cohorts, the no prior diagnosis and the prior diagnosis. And by doing it all online, what you can do is through skip patterns, you can immediately separate these. So you say have you had breast cancer. The women who say yes go down one path and see a whole set of questions. The women who say no never see those questions. The men with breast cancer who come and say — you say are you male or female, and if they're male, we never ask them when their last period was. So you don't have to see all the questions that don't relate to you and you can also make it in such a way that you can almost pre-clean the data because you don't allow the 80-year-old woman to say that she's pregnant. It's just not one of the options. So you can really sort things out at an earlier stage.

We did a rolling admission so the first email was a—this is a beta test we did in last December, and you can see the dates were less than fortuitous, right before Christmas. However, we sent out the first email, then we doubled it for the second email, and then doubled again for the third, fourth, and fifth. So they didn't get five



emails; these are sent out to different people. And you can see as we increased the number of emails going out, we increased the enrollment. In this beta launch, we had 25,414 who signed up within that first week, and the majority of them, not surprisingly, are age 50 to 69. We have a few older women even on this totally online just showing you that older women will do online things as well as younger women. Not surprisingly, it's mostly white with a smattering of ethnicity. This is something we're working on both in the Army and for the HOW study.

Eighteen percent of the women in the beta test were breast cancer survivors which was actually lower than the Army itself and showed that people and healthy women are very eager to participate in finding the answer. We do allow men in the Army of Women and the Health of Women study; we're just not going to change the name, they have to put up with it. We've been putting up with it for years. And we have 28 men in the HOW study, 24 percent of them—or 28 of the men in the HOW study have had breast cancer as well. Ninety percent had one full-term pregnancy, 28 percent are overweight, and 23 percent were obese. This is just sort of a snapshot, but if you look at the women with breast cancer, you see that we have a fair number of young women that were diagnosed before age 45, the major portion is 45 to 54 which is interesting because the median age of breast cancer in this country is actually 64. We have a fair number of women who were within a year or two of diagnosis down here, but we also have 1,273 who are ten years out from their diagnosis or 29 percent. And this is—remember, this is just the beta test. We have 24 percent that actually have in situ cancer so a very high percentage of that, as well as early stage breast cancer and a hardy group of women with metastatic disease who we hear from regularly.

When we compare this to an existing cohort, we're doing this study with Leslie Bernstein's group at City of Hope and they run the California teachers study. So we thought we would just look at recruiting people online like this and how is it different from a standard cohort, recognizing that this is just a small sample of the people we hope to have in the HOW study. So we recruited with one email in December; they recruited through two mailings to 300,000 teachers in 1995 to '96. Our people we directed to registered at a website and fill out the online module. They were sent a 16-page detailed questionnaire. 1,414, eight percent, responded the week before Christmas, completed the module and they have 133,476 who returned their questionnaire.

If you compare in ethnicity, they're a little more diverse than we are. In the teachers study they have higher percentages of other ethnicities than we do. And whether this has to do with the fact that it's online or not, we don't know at this point. If you look at ages, overall they have a higher median age than we do because they have more older people here in this light blue and you might anticipate a higher younger or a skew a little younger for an online cohort.

Reproductive history, I think this represents in fact the way we asked the questions in '95 versus now. I don't think we talked about perimenopause in '95 so we have a lot of perimenopause women in HOW and they were all considered post-menopausal when they were in the teachers study. But other than that, it's about the same. Weight, the HOW beta is a little heavier than the California teachers study but



basically it's about the same. Maybe that's because they were in '95 and now everybody's a little heavier than they were in 1995.

The next part of it—so the full launch of HOW should be—will happen some time in the middle of October. We're on the verge of pulling the plug to everybody. The important thing about HOW is also to involve the public in answering questions. So each module that we ask, we ask the public a question and solicit questions from them, what questions would you like to see asked. And then we also have been approached by particular advocacy groups about the questions they want relevant to their experience, what are the things that they want to know. And this is important because I think too often researchers ask questions that are interesting to them but actually not necessarily interesting to the people who are going through the disease. And this is particularly true, I think, in comparative effectiveness research where we tend to compare things that we have in the chart, the medical record, or we have information on rather than things that are actually relevant to people. So the metastatic group is coming up with questions for their own module. We have an active transsexual group that is very eager to see whether the hormones that they take are increasing breast cancer risk. Nobody's really looked at this. And fertility issues are another big question.

In the first module we asked people what do you think causes breast cancer. And interestingly, genetics was the most common and then environment and then lifestyle. So it sort of reflects that genetics is really not the major, at least in this point in time, thing, and we had a fair number of bad luck in there as well which is probably the most accurate.

So the next step is we're launching in October as I said. We're going to have—in the Army of Women another step will be opting in for other diseases. We've been approached by a lot of other advocacy groups that they want to have a multiple myeloma army and an Alzheimer's army and that really doesn't make a lot of sense because people have more than one disease. So what we are going to do is in the beginning when you sign up for the Army, we'll allow you to opt in I also would like to hear about diabetes studies or I'd also like—and then you can start to segment the list that way. We're working on a way that researchers who don't have the money to do a whole cohort could come up with a module relevant to their issue. We'll collect the data for them, give it to them, and then also keep the data for ourselves, the rent-a-module plan. We're working, as I said, with women to develop the modules and we're also working to be able to recruit for the Army through a mobile phone which we think once we can do that, we think that will actually help in our diversity as well.

So democratizing research needs to address issues that are important to the public, not just the issues that are interesting to the scientists. By including the public in the conduct and the design of the research, we'll increase the scientific literacy of the public and the support of research. When you don't, when you separate them, then you really risk losing your support. The public is ready and willing to participate with the research community. They're really eager to find the answers to clinical problems, and I think we need to get them involved. So sign up for the Army of Women. We need all of you. Encourage your family and friends to register. Submit



your studies and questions, and we'll revolutionize how research is done in this country. Thank you.

Speakers:

Susan Love, M.D.

Susan Love Research Foundation